

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of report (Date of earliest event reported): January 6, 2017

WAVE LIFE SCIENCES LTD.

(Exact name of registrant as specified in its charter)

Singapore
(State or other jurisdiction
of incorporation)

001-37627
(Commission
File Number)

Not Applicable
(IRS Employer
Identification No.)

8 Cross Street #10-00, PWC Building
Singapore 048424
(Address of principal executive offices)

048424
(Zip Code)

Registrant's telephone number, including area code: +65 6236 3388

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 7.01 Regulation FD Disclosure.

From time to time, WAVE Life Sciences Ltd. (the "Company"), presents and/or distributes slides and presentations to the investment community at various industry and other conferences to provide updates and summaries of its business. On January 6, 2017, the Company updated its corporate presentation, which is available on the Investors & Media section of the Company's website at <http://ir.wavelifesciences.com/>. This presentation is attached as Exhibit 99.1 and is incorporated by reference herein.

The information in Item 7.01 of this Form 8-K, including Exhibit 99.1 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On January 6, 2017, the Company issued a press release providing an update on its pipeline. A copy of the press release is attached as Exhibit 99.2 to this Form 8-K and is incorporated by reference herein.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	Corporate presentation of WAVE Life Sciences Ltd., dated as of January 6, 2017
99.2	Press release issued by WAVE Life Sciences Ltd. on January 6, 2017

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

WAVE LIFE SCIENCES LTD.

Date: January 6, 2017

/s/ Keith C. Regnante

Keith C. Regnante
Chief Financial Officer



WAVETM
LIFE SCIENCES

Pure. Precise.
Exceptional, for Patients.

Corporate Presentation

January 6, 2017



Forward Looking Statements

This document contains forward-looking statements. All statements other than statements of historical facts contained in this document, including statements regarding possible or assumed future results of operations, business strategies, development plans, regulatory activities, competitive position, potential growth opportunities, use of proceeds and the effects of competition are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause the actual results, performance or achievements of WAVE Life Sciences Ltd. (the "Company") to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "aim," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this presentation are only predictions. The Company has based these forward-looking statements largely on its current expectations and projections about future events and financial trends that it believes may affect the Company's business, financial condition and results of operations. These forward-looking statements speak only as of the date of this presentation and are subject to a number of risks, uncertainties and assumptions, including those listed under Risk Factors in the Company's Form 10-K and other filings with the SEC, some of which cannot be predicted or quantified and some of which are beyond the Company's control. The events and circumstances reflected in the Company's forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, the Company operates in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that the Company may face. Except as required by applicable law, the Company does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

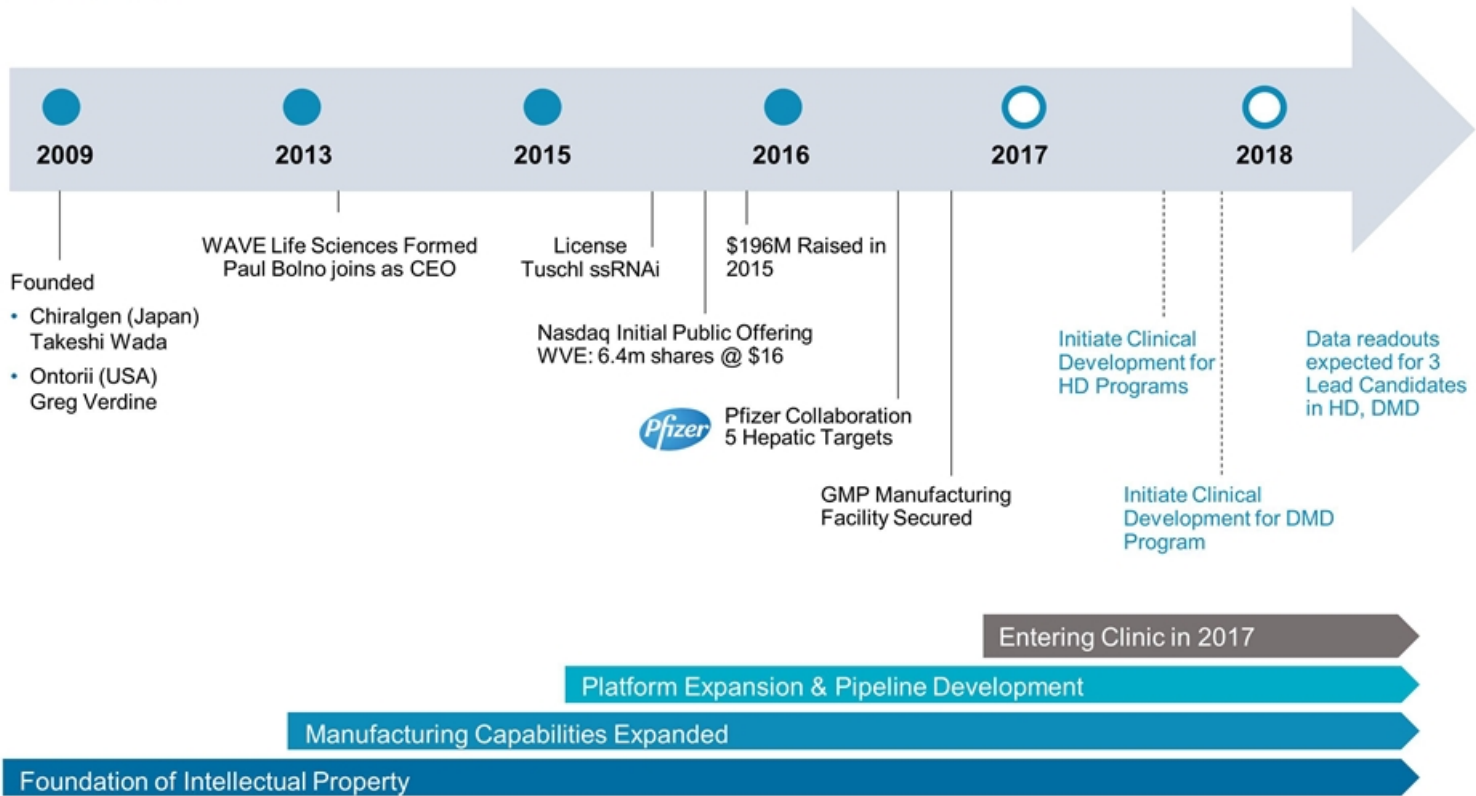
WAVE Life Sciences

Overview

- Genetic medicines company developing targeted nucleic acid therapies for patients impacted by rare diseases
- Rationally designed nucleic acid therapeutics optimized by stereochemistry
- Three lead candidates initiating clinical trials in 2017
- Six development programs by end of 2018
- Core focus and expertise in neurological rare genetic diseases
- Strategic partnerships for non-core assets, addressing multiple therapeutic areas
- Proprietary R&D platform and advanced chemistry: a sustainable engine for future growth
- Cash runway into 2019

WAVE Life Sciences

Overview



WAVE Life Sciences

R&D Exploratory Platform

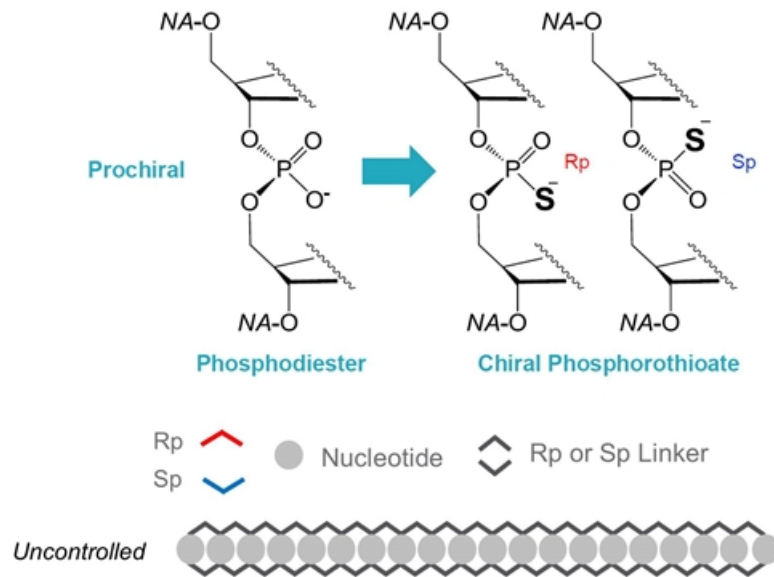
	THERAPEUTIC AREA	DISEASE	TARGET	DISCOVERY	CANDIDATE	CLINICAL	SPRING	SILENCING	
								ALISE SPECIFIC	NON-ALISE SPECIFIC
Core Neurology Portfolio	CNS	HUNTINGTON'S DISEASE	HTT SNP-1	██████████	██████████	Mid 2017	⊗		
			SNP-2	██████████	██████████	Mid 2017	⊗		
			SNP-3	██████████	██████████		⊗		
		SPINAL MUSCULAR ATROPHY	SMN2	██████████	██████████		⊗		
		AMYOTROPHIC LATERAL SCLEROSIS	UNDISCLOSED	██████████	██████████		⊗		
		MYOTONIC DYSTROPHY TYPE 1	DMPK SNP-1	██████████	██████████		⊗		
			SNP-2	██████████	██████████		⊗		
	MUSCLE	DUCHENNE MUSCULAR DYSTROPHY	DYSTROPHIN EXON 51	██████████	██████████	2H 2017	⊗		
			EXON 45	██████████	██████████		⊗		
			EXON 53	██████████	██████████		⊗		
EXON 44			██████████	██████████		⊗			
		ACTIVIN RECEPTOR	██████████	██████████				⊗	
EYE	RARE GENETIC	UNDISCLOSED	██████████	██████████				⊗	
		UNDISCLOSED	██████████	██████████		⊗			
LIVER	RARE GENETIC	UNDISCLOSED	██████████	██████████				⊗	
		UNDISCLOSED	██████████	██████████				⊗	
	METABOLIC	APOC3	██████████	██████████					⊗
		UNDISCLOSED	██████████	██████████					⊗
		UNDISCLOSED	██████████	██████████				⊗	
SKIN	EPIDERMOLYSIS BULLOSA SIMPLEX	KRT14 SNP-1	██████████	██████████				⊗	
		SNP-2	██████████	██████████				⊗	
	RARE GENETIC	UNDISCLOSED	██████████	██████████				⊗	
GI	IBD	SMAD7	██████████	██████████				⊗	
		UNDISCLOSED	██████████	██████████				⊗	

Nucleic Acid Therapeutics

Traditional Approach

PS Modifications Introduce Chiral Centers

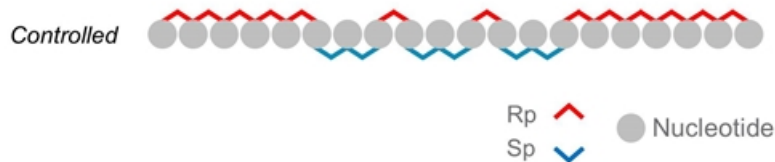
An enormous number of permutations exist, often resulting in over 500,000 different molecules in every dose (e.g., 2^{19} Antisense and Exon Skipping)



Controlling PS Linkages of Stereoisomers

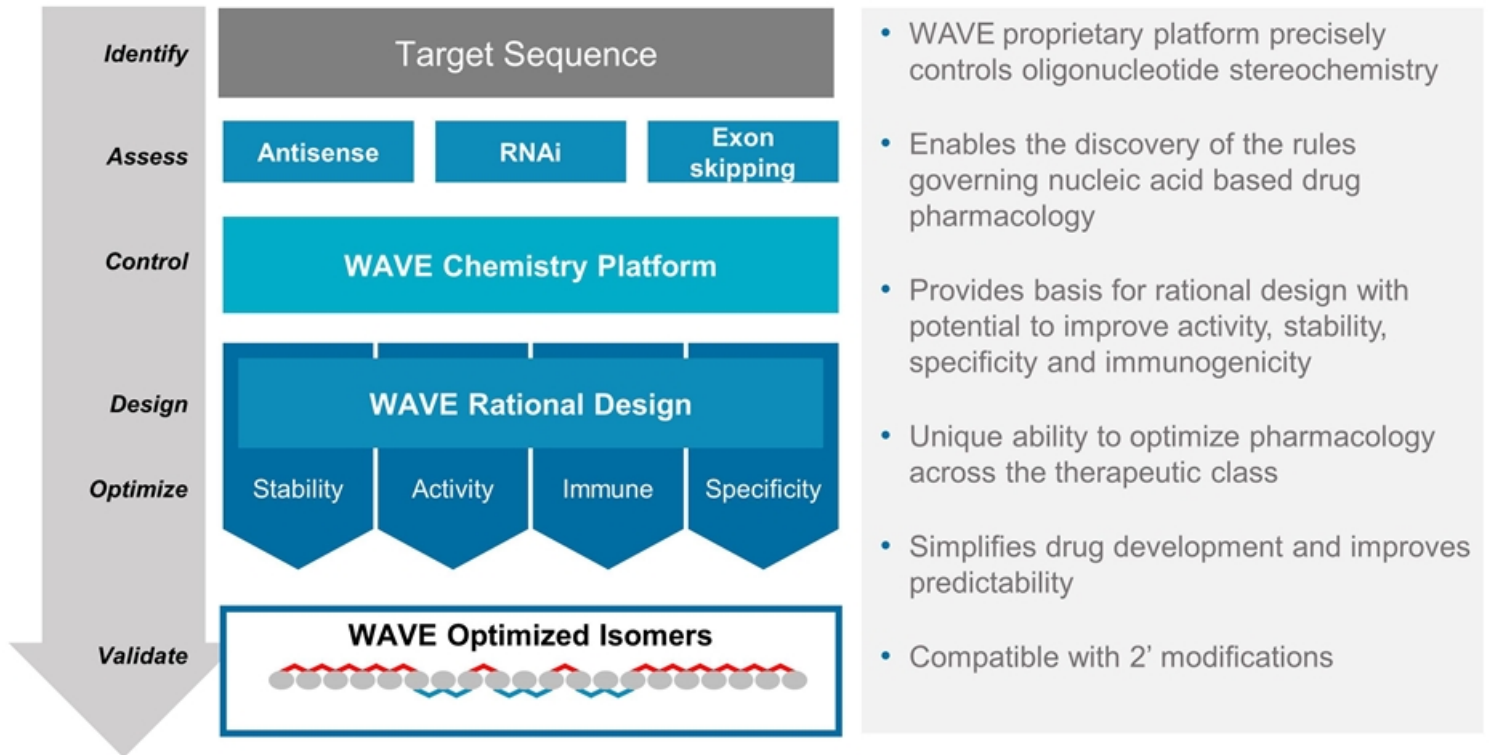
Precisely designing and securing sequence improves stability, potency, specificity, and immunogenicity

Stereopure PS Linkages: PS Placement by design



- WAVE platform enables the rational design, optimization and production of nucleic acid therapeutics, beginning with the control of stereochemistry
- By controlling the orientation of the chiral linkages in phosphorothioate (PS) backbone modifications, WAVE is able to optimize the interaction between a nucleic acid therapy and various enzymes to improve pharmacology

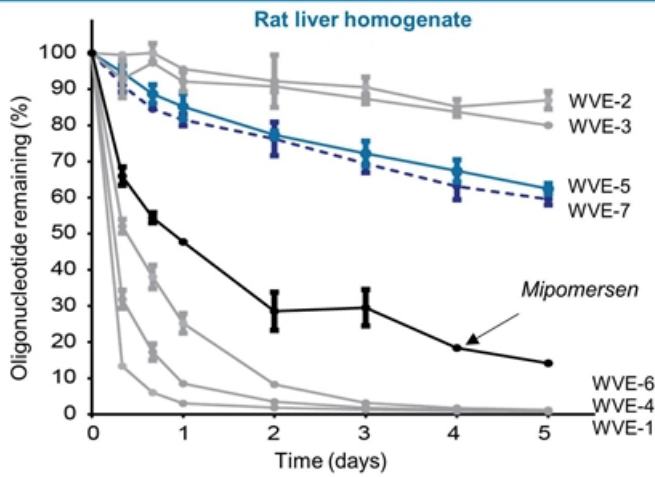
Conventional wisdom of small molecule drug discovery applied to nucleic acid therapeutics



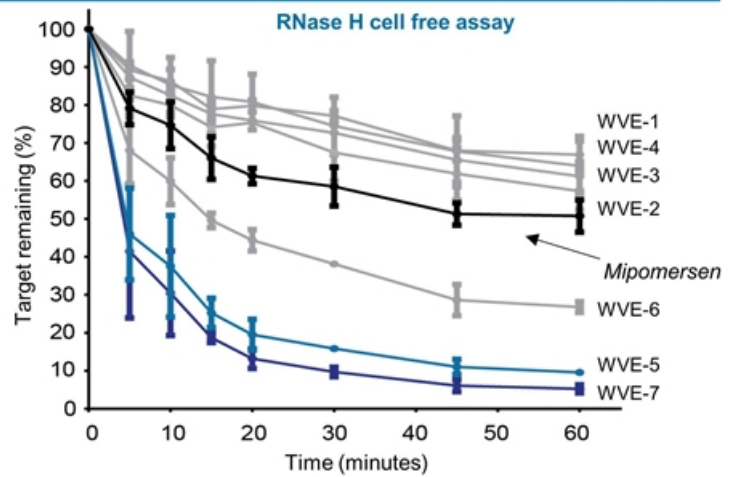
R&D Platform

WAVE chemistry enables increased stability and activity

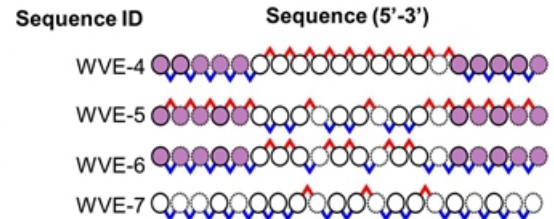
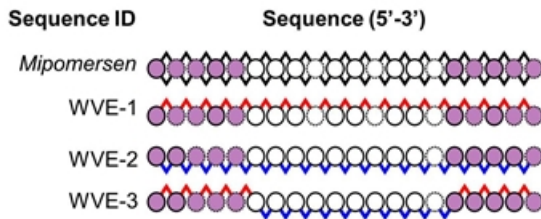
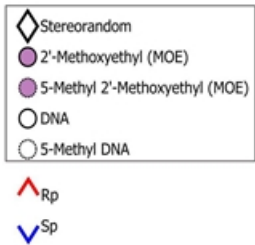
Stability



Activity



Stereopure WAVE Mipomersen Isomers

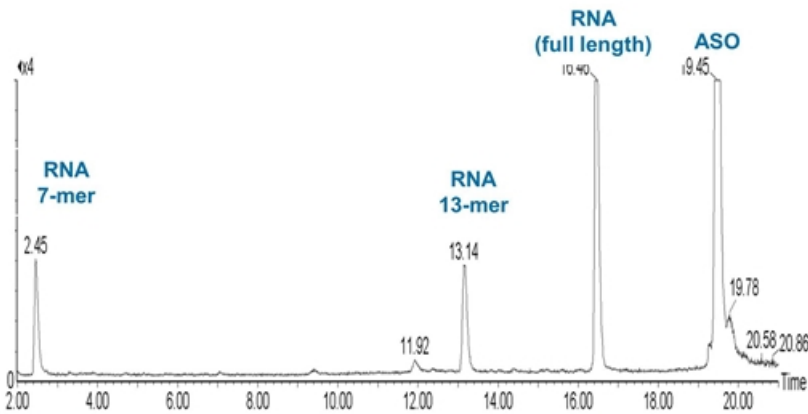
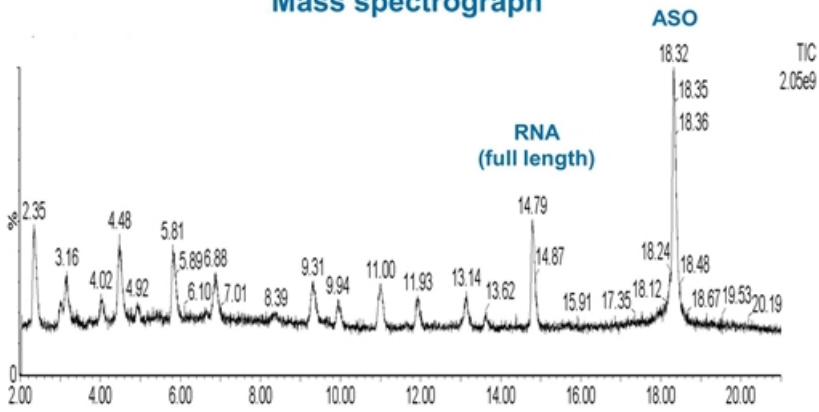


R&D Platform

WAVE chemistry allows highly specific targeting

Specificity

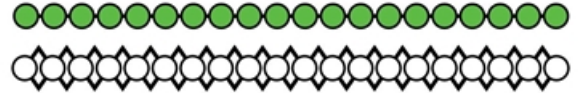
Mass spectrograph



Stereorandom

Multiple cleavage sites

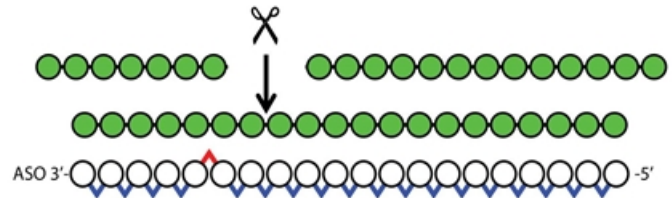
- 2.35min: 7mer
- 3.16min: 8mer, P-6mer
- 4.58min: P-7mer
- 5.91min: P-8mer
- 7.19min: 12mer
- 9.55min: 13mer
- 10.13min: P-11mer
- 11.14min: P-12mer, 14mer
- 12.11min: P-13mer
- 13.29min: P-14mer
- Others



WAVE stereopure

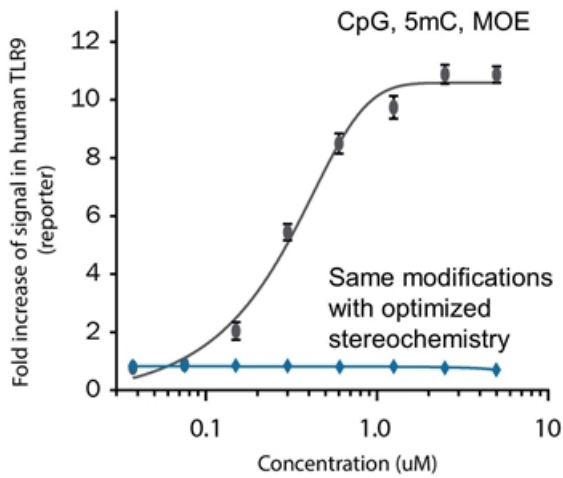
Single defined cleavage site

- 2.45min: P-7mer
- 13.14: 13-mer

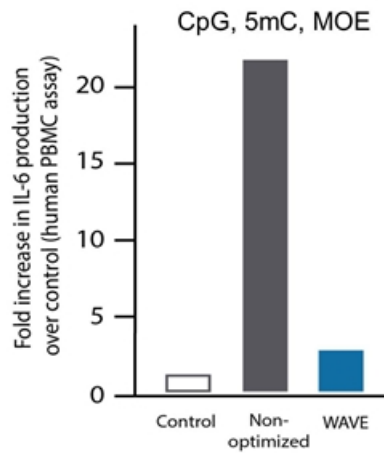


Immunogenicity

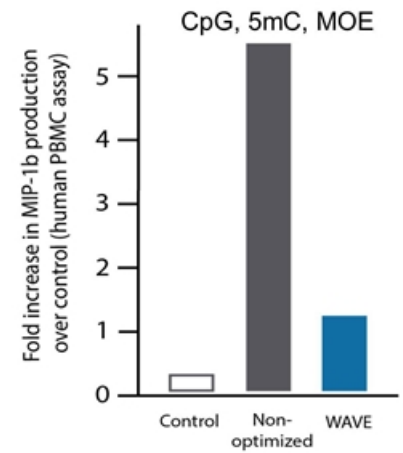
Human TLR9 assay



PBMC IL-6 activation



PBMC MIP-1b activation



- Conventional wisdom: 5-methyl C (5mC) and 2' modification is sufficient to avoid immune activation
- However, substantial immune activation exists within highly stable compounds despite the incorporation of these modifications
- WAVE chemistry platform enables reduced activation of the immune system
- Human TLR9 reporter assay and human PBMC cytokine panel (IL-6 and MIP-1b are key cytokines in B-cell and macrophage activation, respectively)

WAVE Intellectual Property

WAVE Stereochemistry Patents Granted and Pending

- Foundational Chemistry
- Chiral Control and Design
- Platform
- Candidate Specific IP

Co-exclusive license holder for single-strand RNAi (ssRNAi) patent estate

- Martinez J, Patkaniowska A, Urlaub H, Lührmann R, Tuschl T. Single-stranded antisense siRNAs guide target RNA cleavage in RNAi. *Cell*. 2002;110:563–574.
- License includes 19-29 nucleotides molecules; RNAi mechanism; various chemical modifications

License to Pfizer hepatic targeting technology

Single Strand RNAi

New modalities

- In June 2015, WAVE became the co-exclusive license holder (with Ionis Pharmaceuticals) to the single-strand RNAi patent estate (Tuschl, Zamore)
- Includes 19-29 nucleotides molecules; RNAi mechanism; various chemical modifications
- Single-stranded RNAi requires different design rules from double-stranded RNAi formats
- When properly optimized, single-stranded RNAi has comparable or greater potency than double-stranded RNAi formats
- Stereopure modifications are expected to provide further enhancements to pharmacology

United States Patent Zamore et al.		(19) Patent No.: US 8,720,636 B2
		(11) Date of Patent: May 20, 2014
(54) COMPOSITIONS FOR SILENCING AND MODIFICATION OF GENE EXPRESSION	30100162 30100163 30100164 30100165 30100166 30100167 30100168 30100169 30100170 30100171 30100172 30100173 30100174 30100175 30100176 30100177 30100178 30100179 30100180 30100181 30100182 30100183 30100184 30100185 30100186 30100187 30100188 30100189 30100190 30100191 30100192 30100193 30100194 30100195 30100196 30100197 30100198 30100199 30100200	61201 Tsuchida et al. 61202 Tsuchida et al. 61203 Tsuchida et al. 61204 Tsuchida et al. 61205 Tsuchida et al. 61206 Tsuchida et al. 61207 Tsuchida et al. 61208 Tsuchida et al. 61209 Tsuchida et al. 61210 Tsuchida et al. 61211 Tsuchida et al. 61212 Tsuchida et al. 61213 Tsuchida et al. 61214 Tsuchida et al. 61215 Tsuchida et al. 61216 Tsuchida et al. 61217 Tsuchida et al. 61218 Tsuchida et al. 61219 Tsuchida et al. 61220 Tsuchida et al. 61221 Tsuchida et al. 61222 Tsuchida et al. 61223 Tsuchida et al. 61224 Tsuchida et al. 61225 Tsuchida et al. 61226 Tsuchida et al. 61227 Tsuchida et al. 61228 Tsuchida et al. 61229 Tsuchida et al. 61230 Tsuchida et al. 61231 Tsuchida et al. 61232 Tsuchida et al. 61233 Tsuchida et al. 61234 Tsuchida et al. 61235 Tsuchida et al. 61236 Tsuchida et al. 61237 Tsuchida et al. 61238 Tsuchida et al. 61239 Tsuchida et al. 61240 Tsuchida et al. 61241 Tsuchida et al. 61242 Tsuchida et al. 61243 Tsuchida et al. 61244 Tsuchida et al. 61245 Tsuchida et al. 61246 Tsuchida et al. 61247 Tsuchida et al. 61248 Tsuchida et al. 61249 Tsuchida et al. 61250 Tsuchida et al. 61251 Tsuchida et al. 61252 Tsuchida et al. 61253 Tsuchida et al. 61254 Tsuchida et al. 61255 Tsuchida et al. 61256 Tsuchida et al. 61257 Tsuchida et al. 61258 Tsuchida et al. 61259 Tsuchida et al. 61260 Tsuchida et al. 61261 Tsuchida et al. 61262 Tsuchida et al. 61263 Tsuchida et al. 61264 Tsuchida et al. 61265 Tsuchida et al. 61266 Tsuchida et al. 61267 Tsuchida et al. 61268 Tsuchida et al. 61269 Tsuchida et al. 61270 Tsuchida et al. 61271 Tsuchida et al. 61272 Tsuchida et al. 61273 Tsuchida et al. 61274 Tsuchida et al. 61275 Tsuchida et al. 61276 Tsuchida et al. 61277 Tsuchida et al. 61278 Tsuchida et al. 61279 Tsuchida et al. 61280 Tsuchida et al. 61281 Tsuchida et al. 61282 Tsuchida et al. 61283 Tsuchida et al. 61284 Tsuchida et al. 61285 Tsuchida et al. 61286 Tsuchida et al. 61287 Tsuchida et al. 61288 Tsuchida et al. 61289 Tsuchida et al. 61290 Tsuchida et al. 61291 Tsuchida et al. 61292 Tsuchida et al. 61293 Tsuchida et al. 61294 Tsuchida et al. 61295 Tsuchida et al. 61296 Tsuchida et al. 61297 Tsuchida et al. 61298 Tsuchida et al. 61299 Tsuchida et al. 61300 Tsuchida et al.
(57) Inventor: Phillip D. Zamore, Nathan M. Glavin, Gregory S. Storz, Mitchell S. Hildebrand, James J. R. Taylor, et al.		

United States Patent Tsuchi et al.		(19) Patent No.: US 8,101,340 B2
		(11) Date of Patent: Jun. 24, 2012
(54) RNAI-MODULATING AGENTS AND METHODS OF USE	30100201 30100202 30100203 30100204 30100205 30100206 30100207 30100208 30100209 30100210 30100211 30100212 30100213 30100214 30100215 30100216 30100217 30100218 30100219 30100220 30100221 30100222 30100223 30100224 30100225 30100226 30100227 30100228 30100229 30100230 30100231 30100232 30100233 30100234 30100235 30100236 30100237 30100238 30100239 30100240 30100241 30100242 30100243 30100244 30100245 30100246 30100247 30100248 30100249 30100250	61301 Tsuchida et al. 61302 Tsuchida et al. 61303 Tsuchida et al. 61304 Tsuchida et al. 61305 Tsuchida et al. 61306 Tsuchida et al. 61307 Tsuchida et al. 61308 Tsuchida et al. 61309 Tsuchida et al. 61310 Tsuchida et al. 61311 Tsuchida et al. 61312 Tsuchida et al. 61313 Tsuchida et al. 61314 Tsuchida et al. 61315 Tsuchida et al. 61316 Tsuchida et al. 61317 Tsuchida et al. 61318 Tsuchida et al. 61319 Tsuchida et al. 61320 Tsuchida et al. 61321 Tsuchida et al. 61322 Tsuchida et al. 61323 Tsuchida et al. 61324 Tsuchida et al. 61325 Tsuchida et al. 61326 Tsuchida et al. 61327 Tsuchida et al. 61328 Tsuchida et al. 61329 Tsuchida et al. 61330 Tsuchida et al. 61331 Tsuchida et al. 61332 Tsuchida et al. 61333 Tsuchida et al. 61334 Tsuchida et al. 61335 Tsuchida et al. 61336 Tsuchida et al. 61337 Tsuchida et al. 61338 Tsuchida et al. 61339 Tsuchida et al. 61340 Tsuchida et al. 61341 Tsuchida et al. 61342 Tsuchida et al. 61343 Tsuchida et al. 61344 Tsuchida et al. 61345 Tsuchida et al. 61346 Tsuchida et al. 61347 Tsuchida et al. 61348 Tsuchida et al. 61349 Tsuchida et al. 61350 Tsuchida et al. 61351 Tsuchida et al. 61352 Tsuchida et al. 61353 Tsuchida et al. 61354 Tsuchida et al. 61355 Tsuchida et al. 61356 Tsuchida et al. 61357 Tsuchida et al. 61358 Tsuchida et al. 61359 Tsuchida et al. 61360 Tsuchida et al. 61361 Tsuchida et al. 61362 Tsuchida et al. 61363 Tsuchida et al. 61364 Tsuchida et al. 61365 Tsuchida et al. 61366 Tsuchida et al. 61367 Tsuchida et al. 61368 Tsuchida et al. 61369 Tsuchida et al. 61370 Tsuchida et al. 61371 Tsuchida et al. 61372 Tsuchida et al. 61373 Tsuchida et al. 61374 Tsuchida et al. 61375 Tsuchida et al. 61376 Tsuchida et al. 61377 Tsuchida et al. 61378 Tsuchida et al. 61379 Tsuchida et al. 61380 Tsuchida et al. 61381 Tsuchida et al. 61382 Tsuchida et al. 61383 Tsuchida et al. 61384 Tsuchida et al. 61385 Tsuchida et al. 61386 Tsuchida et al. 61387 Tsuchida et al. 61388 Tsuchida et al. 61389 Tsuchida et al. 61390 Tsuchida et al. 61391 Tsuchida et al. 61392 Tsuchida et al. 61393 Tsuchida et al. 61394 Tsuchida et al. 61395 Tsuchida et al. 61396 Tsuchida et al. 61397 Tsuchida et al. 61398 Tsuchida et al. 61399 Tsuchida et al. 61400 Tsuchida et al.
(57) Inventor: Thomas Tsuchi, Thomas Tsuchi, et al.		

Abstract: Single-stranded antisense siRNAs are described. The siRNAs are single-stranded and are capable of forming a duplex with a target RNA. The siRNAs are capable of forming a duplex with a target RNA in the presence of a protein, such as a protein kinase. The siRNAs are capable of forming a duplex with a target RNA in the presence of a protein, such as a protein kinase, and are capable of forming a duplex with a target RNA in the presence of a protein, such as a protein kinase, and are capable of forming a duplex with a target RNA in the presence of a protein, such as a protein kinase. The siRNAs are capable of forming a duplex with a target RNA in the presence of a protein, such as a protein kinase, and are capable of forming a duplex with a target RNA in the presence of a protein, such as a protein kinase. The siRNAs are capable of forming a duplex with a target RNA in the presence of a protein, such as a protein kinase, and are capable of forming a duplex with a target RNA in the presence of a protein, such as a protein kinase.

“Considering the feasibility of modulating the stability and uptake properties of single-stranded RNAs, 5'-phosphorylated single-stranded antisense siRNAs may further expand the utility of RNAi-based gene silencing technology as tool for functional genomics as well as therapeutic applications.”

Martinez J, Patkaniowska A, Urlaub H, Lührmann R, Tuschl T. Single-stranded antisense siRNAs guide target RNA cleavage in RNAi. *Cell*. 2002;110:563–574.

WAVE Advantages

Summary

Scalable Synthesis



Superior Pharmacology



Applicable Across Modalities



- Continue to meet demand
- IND enabling studies
- GMP clinical trial supply
- Comparable cost of goods
- Potential cost-per-patient advantages (dose and schedule)

- Rational design of single drugs
- Increased activity
- Increased stability
- Increased specificity
- Reduced immune activation
- Compatible with targeting moieties (GalNAc, others)
- Other areas in development

- Antisense (RNase H)
- Exon skipping
- RNAi single-strand (Ago2)
- Guide-strand (CRISPR)
- Genetic medicines toolkit
- Other areas in development

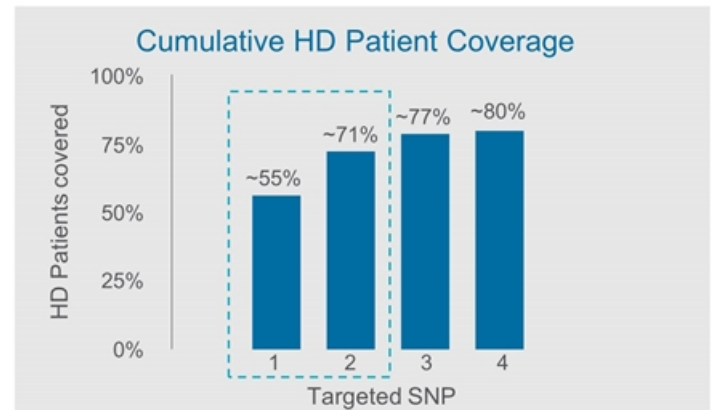
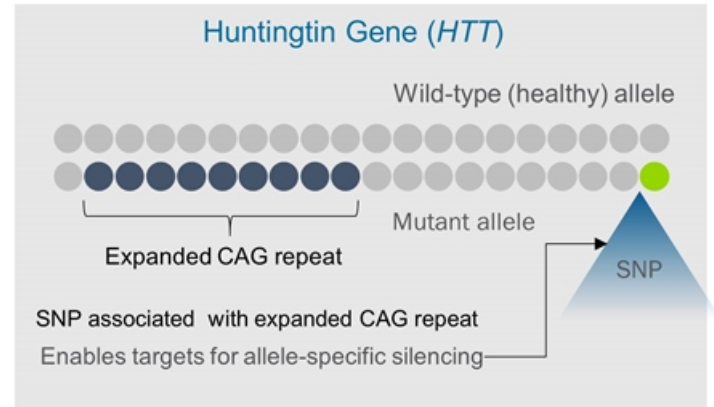
Huntington's Disease (HD)

Background

- Autosomal dominant disorder, characterized by chorea, psychiatric illness and cognitive decline
- Expanded CAG triplet repeat in HTT gene results in production of mutant HTT (mHTT) protein; accumulation of mHTT causes progressive loss of neurons in the brain¹
- Approximately 30,000 individuals have symptomatic HD in the United States
- No approved disease-modifying therapies available
- Wild type (healthy) HTT protein critical for neuronal function, and suppression may have detrimental long-term consequences²⁻⁸

WAVE Approach

- Lower mHTT gene transcript alone, while leaving healthy HTT relatively intact
- Target single nucleotide polymorphisms (SNPs) associated with mHTT gene to provide an approach to allele-specific gene silencing⁹

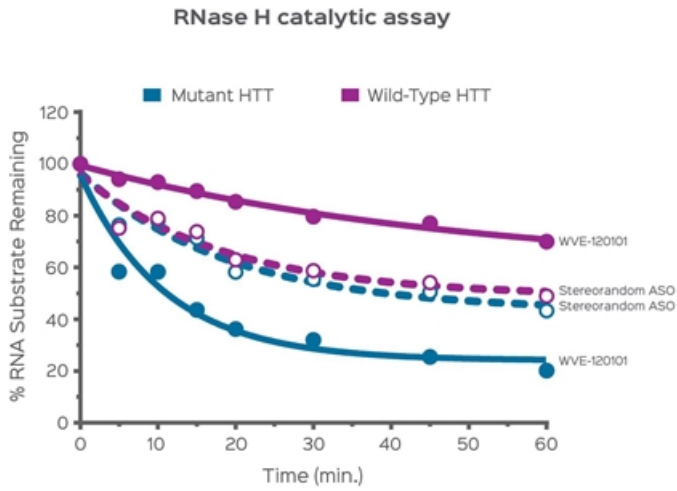


¹Sturrock A, Leavitt BR. *J Geriatr Psychiatry Neurol.* 2010;23:243-259. ²Auerbach W, et al. *Hum Mol Genet.* 2001;10:2515-2523. ³Dragatsis I, et al. *Nat Genet.* 2000;26:300-306. ⁴Leavitt BR, et al. *J Neurochem.* 2006;96:1121-1129. ⁵Nasir J, et al. *Cell.* 1995;81:811-823. ⁶Reiner A, et al. *J Neurosci.* 2001;21:7608-7619. ⁷White JK, et al. *Nat Genet.* 1997;17:404-410. ⁸Zeitlin S, et al. *Nat Genet.* 1995;11:155-163. ⁹Carroll JB, et al. *Mol Ther.* 2011;19:2178-2185.

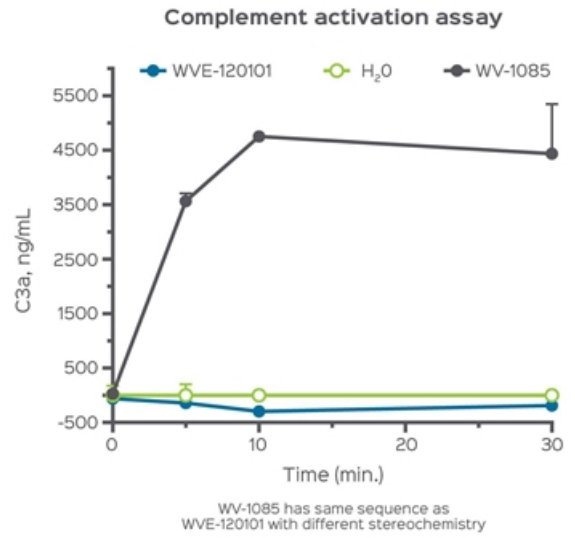
Huntington's Disease

WVE-120101 Selectively Cleaves mHTT RNA

Selective Knockdown of mHTT Allele



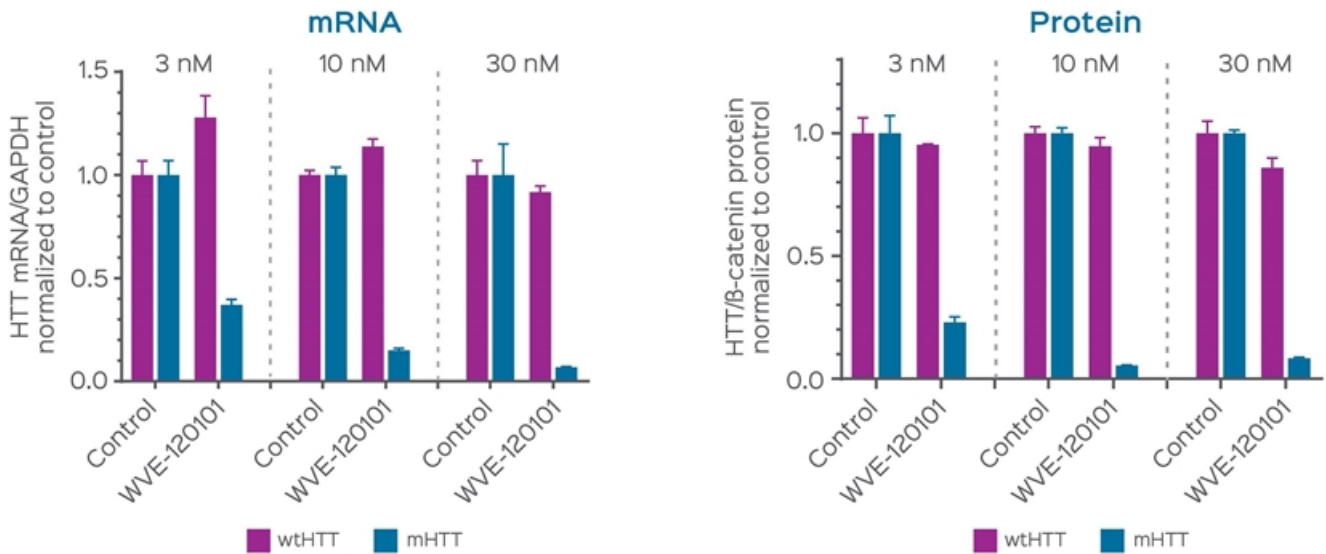
Reduced Complement Immune Response



Huntington's Disease

WVE-120101 Selectively Reduces mHTT mRNA and Protein

Reporter Cell Line*

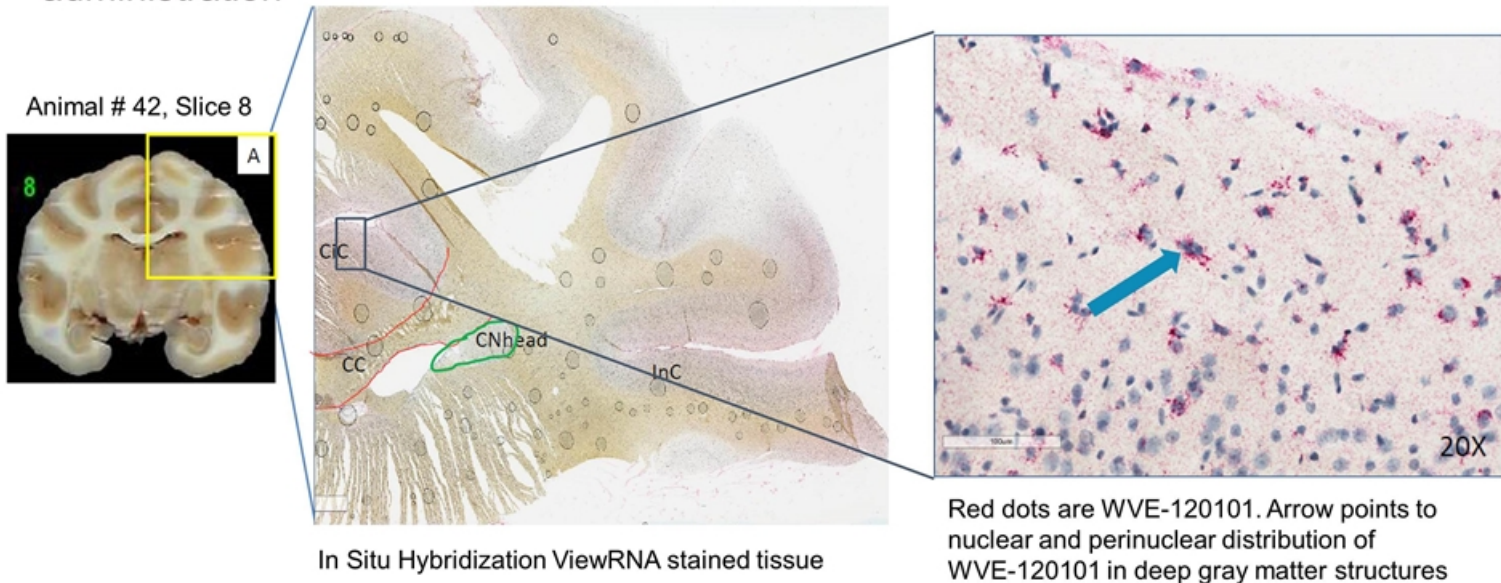


*These results were replicated in a patient-derived cell line

Huntington's Disease

Distribution of WVE-120101 in Cynomolgus NHP Brain

- Stereochemistry enables improved protein binding and distribution
- ViewRNA depicting perinuclear distribution of WVE-120101 (red) in non-human primate (NHP) deep gray matter structures following intrathecal administration
- WVE-120101 detectable in deep gray matter structures following intrathecal administration

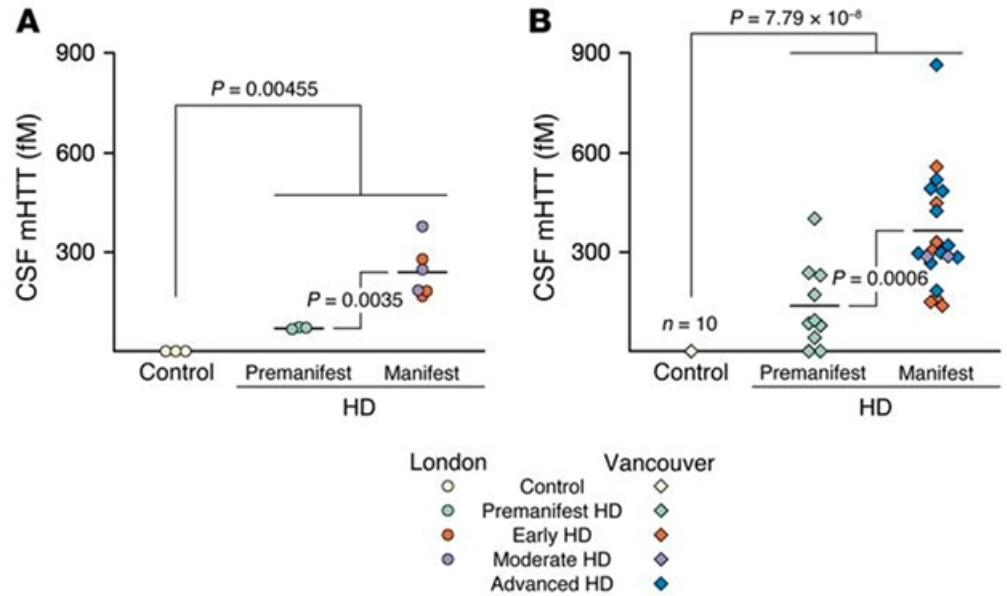


Huntington's Disease

Single Molecule Counting mHTT

Advancements in Huntington's disease research allow for better quantification and measurement of mutant huntingtin

- Novel immunoassay allows for selective detection of mutant huntingtin in CSF
- Level of mHTT detected associated with time to onset, diminished cognitive and motor function



Source: Wild E, et al. Quantification of mutant huntingtin protein in cerebrospinal fluid from Huntington's disease patients. J Clin Invest. 2015;125:1979–1986. Edward Wild, MA MB BChir PhD MRCP Principal Investigator at UCL Institute of Neurology and Consultant Neurologist at the National Hospital for Neurology and Neurosurgery, London

Huntington's Disease

Clinical Development Update

Refile IND for WVE-120101 and file IND for WVE-120102 in 1H 2017 with updated clinical protocols, accelerating time to multi-ascending dose (MAD) studies and potentially reducing time to proof-of-concept (POC)

- Updated plan informed by discussions with the FDA and new supportive data from multi-dose animal toxicology studies
- Updated plan includes moving straight to two simultaneous multi-ascending-dose (MAD) studies, potentially accelerating time to proof-of-concept
- Clinical Trial Applications in Europe on track for 1H 2017
- First-in-patient dosing for both WVE-120101 (SNP-1) and WVE-120102 (SNP-2) trials expected mid-year 2017

Huntington's Disease

Clinical Development Update

Updated Clinical Trial Design for WVE-120101 and WVE-120102

- Two parallel global placebo-controlled MAD trials targeting SNP-1 and SNP-2, respectively
- Primary Objective: Assess safety and tolerability of intrathecal doses in early manifest HD patients
- Additional Objectives: Exploratory pharmacokinetic, pharmacodynamic, clinical and MRI endpoints
- Patient SNP determination (SNP-1, SNP-2, other) at pre-screening visit
- Approximately 60 patients per trial
- Key inclusion criteria: Age ≥ 25 to ≤ 65 , Stage I or Stage II Huntington's disease

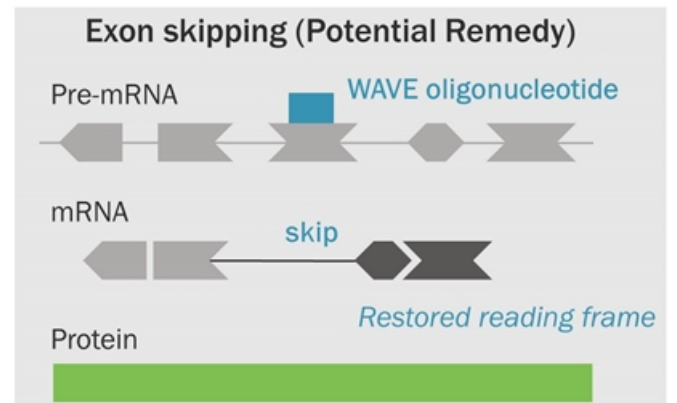
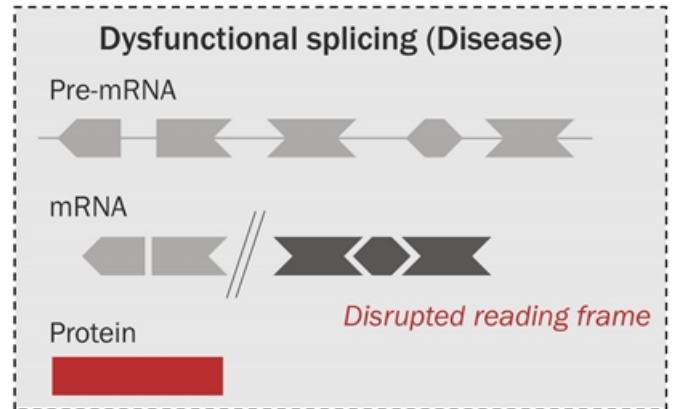
Duchenne Muscular Dystrophy (DMD)

The Disease

- Fatal X-linked genetic neuromuscular disorder caused by reduction of functional dystrophin
- 1 in 3,500 boys worldwide are born with DMD of which 13% carry mutations in Exon 51

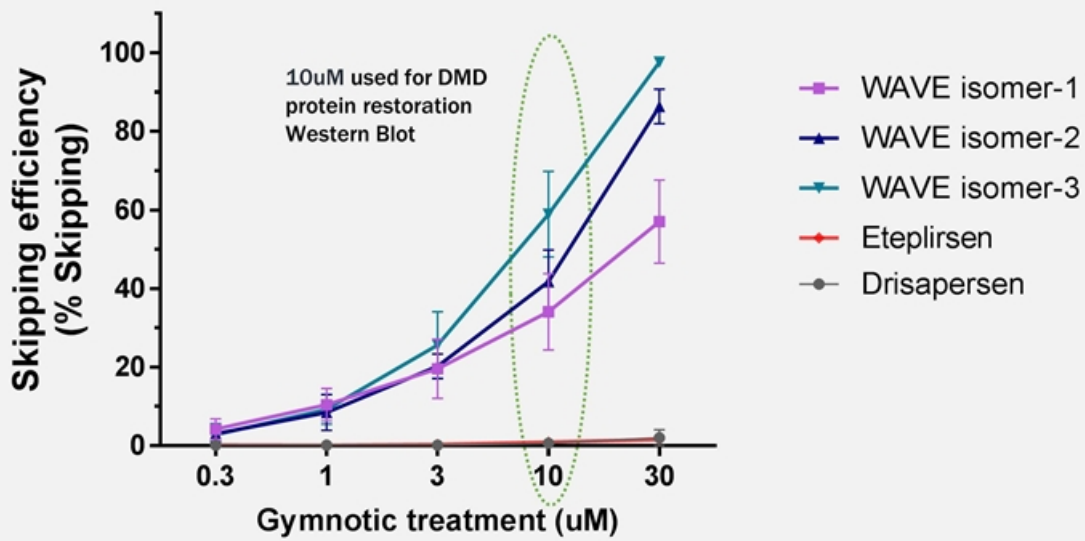
Our Approach

- Partial restoration of dystrophin production is expected to result in therapeutic benefit
- Exon-skipping antisense approaches may enable production of functional dystrophin protein
- WAVE stereopure chemistry has potential to address limitations of current approaches



Duchenne Muscular Dystrophy

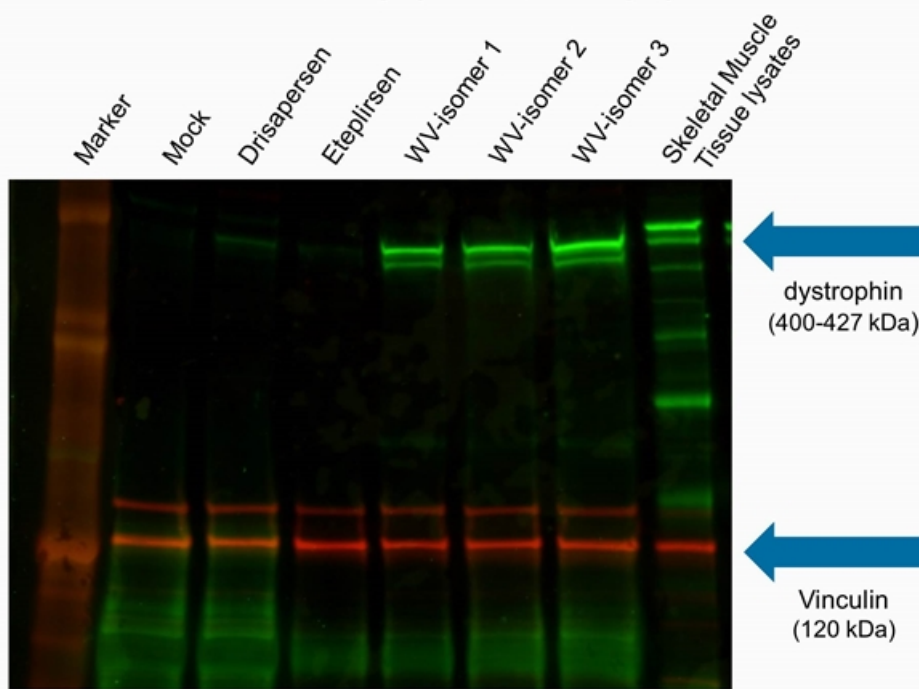
Dose Response on Skipping Efficiency (mRNA, in vitro)
(4 Days)



- RNA skipping determined by quantitative RT-PCR
- WAVE isomers demonstrated a dose-dependent increase in skipping efficiency

Duchenne Muscular Dystrophy

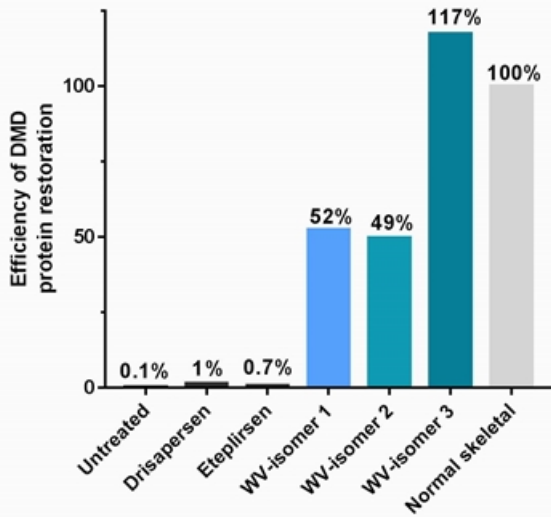
Enhanced Protein Restoration using WAVE Chemistry (10uM, 6 Days)



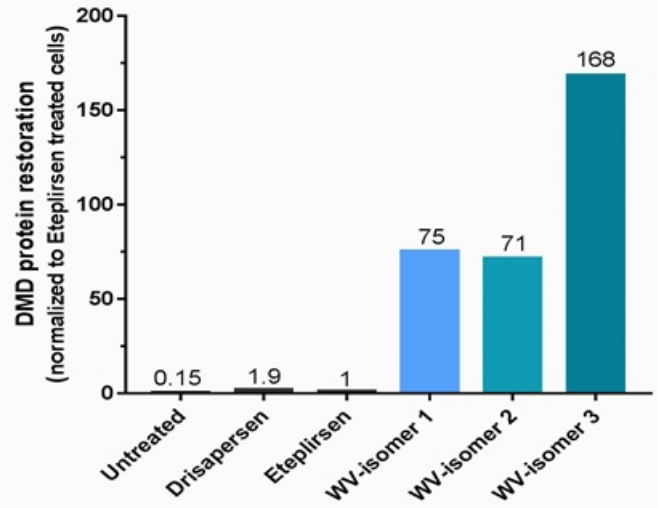
- DMD protein restoration by Western Blot in patient-derived myotubes
- Free uptake at 10uM concentration of each compound with no transfection agent
- Extent of dystrophin protein restoration in vitro was quantified to be between 50-100% of normal skeletal muscle tissue lysates, as compared to about 1% by drisapersen or eteplirsen at this concentration

Duchenne Muscular Dystrophy

Percentage of DMD Protein Restoration Compared to Normal Skeletal Muscle



Fold Increase of DMD Protein Restoration Compared to Eteplirsen



Duchenne Muscular Dystrophy

Clinical Development Update

Candidate selected for DMD Exon 51, WVE-210201 (WV-isomer 1)

- Clinical trials on track to initiate 2H 2017
- Protocol development in collaboration with DMD community
- Trials to include ambulatory and non-ambulatory patients
- Patients previously treated with other exon skipping therapies will not be excluded
- Measurement of dystrophin via standardized Western Blot
- Initiation of GMP manufacturing

WAVE Manufacturing Capabilities

- GMP manufacturing facility leased in Lexington, MA
- Increases control and visibility of our manufacturing supply chain, with potential commercial-scale capabilities by 2019
- 90,000 square foot facility to support future growth
- Supplements existing Cambridge headquarters and facilities
- Facility expected to be occupied 2Q 2017



2017 Upcoming Catalysts

Initiating Three Clinical Programs in 2017

- Initiate two clinical trials in Huntington's disease mid-2017
 - Potential to be first two allele-specific disease-modifying therapies
- Initiate clinical trial in DMD 2H 2017
 - First stereopure oligonucleotide targeting Exon 51 with potential to be best-in-class
- Nominate three additional proprietary therapeutic candidates to progress to clinic
- Initiate in-house GMP production of stereopure oligonucleotide candidates



WAVE Life Sciences 2017 Pipeline Update

Three Lead Neurology Programs to Enter Clinic in 2017

CAMBRIDGE, Mass., January 6, 2016 – WAVE Life Sciences Ltd. (NASDAQ: WVE), a genetic medicines company focused on developing targeted therapies for patients impacted by rare diseases, today announced updates to its clinical pipeline for 2017.

“2017 will be an important year for WAVE as we transition our two lead candidates in Huntington’s disease and our exon-skipping candidate in Duchenne Muscular Dystrophy into clinical trials,” said Paul Bolno, M.D., MBA, President and Chief Executive Officer of WAVE Life Sciences. “Furthermore, we plan to select three additional proprietary candidates this year which will keep us on track to initiate six development programs by the end of 2018, each with the potential to make a meaningful impact to patients with rare genetic diseases.”

Updated clinical development plan for lead Huntington’s disease (HD) programs WVE-120101 and WVE-120102

Informed by discussions with the FDA and with supportive interim data from ongoing multi-dose toxicology studies, WAVE intends to refile its Investigational New Drug (IND) Application for WVE-120101 (SNP-1) and to file its IND for WVE-120102 (SNP-2) in the first half of 2017. The company’s initial plan was to complete a single-ascending-dose phase prior to initiation of the multi-dose portion of the trial. With the updated trial design, the company intends to move straight to two simultaneous multi-ascending-dose (MAD) studies, potentially accelerating time to proof-of-concept.

As part of the company’s HD global development strategy, WAVE remains on track to file a Clinical Trial Application (CTA) in Europe in the first half of 2017. Both SNP-1 and SNP-2 allele-specific HD programs are expected to enter the clinic in mid-2017.

WVE-120101 and WVE-120102 each target a distinct patient population, which together account for over two-thirds of the HD population. Each therapeutic candidate is designed to selectively silence mRNA transcript produced by the disease-causing mutant huntingtin (HTT) allele in order to reduce the mutant HTT protein while leaving the healthy HTT allele intact to produce normal functioning protein. If approved, WVE-120101 and WVE-120102 would be the first allele-specific therapies for Huntington’s disease patients. Huntington’s disease is an autosomal dominant genetic disorder, involving the HTT gene, characterized by chorea, psychiatric illness and cognitive decline. HD is a devastating condition that is invariably fatal affecting over 30,000 symptomatic individuals in the United States alone, with no approved disease-modifying therapies currently available.

Duchenne Muscular Dystrophy program entering clinic in 2H 2017

WAVE has selected its stereopure exon-skipping candidate, WVE-210201, to target deletions of Exon 51. Pre-clinical quantitative Western blot studies of WAVE’s DMD Exon 51 candidate demonstrated 52% dystrophin protein restoration as compared with normal skeletal muscle tissue lysates, versus approximately 1% when testing other exon-skipping therapies. WAVE is developing clinical trial protocol in collaboration with the DMD community and intends to include both ambulatory and non-ambulatory the patients in the study as well as those previously treated with other exon skipping therapies. GMP manufacturing is underway to support planned clinical trials to ensure adequate supply for current and planned studies. The company is on track to initiate a global clinical program in the second half of 2017.

Continued progress unlocking value in adjacent therapeutic areas

WAVE continues to make progress under its collaboration with Pfizer to develop genetically targeted therapies for the treatment of metabolic diseases, including NASH and NAFLD, with three programs advancing through lead-optimization, including ApoC-III programs. The collaboration leverages WAVE’s stereochemistry platform across antisense and RNAi modalities and incorporates GalNAc and Pfizer’s hepatic targeting technology. The remaining two Pfizer collaboration programs are expected to commence by November 2017.

Establishing internal GMP manufacturing capabilities

To provide internal GMP manufacturing capabilities and increase control and visibility of our manufacturing supply chain, WAVE recently signed a lease for a manufacturing facility of approximately 90,000 square feet in Lexington, MA. This new facility supplements WAVE's existing Cambridge, MA headquarters, supports growth and secures availability of drug product for current and future development activities and potential commercial-scale manufacturing.

About WAVE Life Sciences

At WAVE Life Sciences, we are driven by an unwavering passion and commitment to deliver on our mission of confronting challenging diseases by developing transformational therapies and empowering patients. We are utilizing our innovative and proprietary synthetic chemistry drug development platform to design, develop and commercialize rationally redesigned nucleic acid therapeutics that precisely target the underlying cause of rare and other serious genetically defined diseases. Given the versatility of our chemistry platform, WAVE's deep, diverse pipeline spans multiple modalities including antisense, exon-skipping, and single-stranded RNAi. For more information, please visit www.wavelifesciences.com.

Forward Looking Information

This press release contains forward-looking statements concerning our goals, beliefs, expectations, strategies, objectives and plans, and other statements that are not necessarily based on historical facts, including statements regarding the following: the anticipated timing of our IND filings and the commencement of our clinical trials; the design and anticipated goals of our clinical trials; the future performance and results of our programs in clinical trials; the progress and potential benefits of our collaborations with partners; our identification of future candidates and their therapeutic potential; the anticipated therapeutic benefits of stereopure therapies compared to other therapies; our advancing of therapies across multiple modalities and the anticipated benefits of that strategy; our future growth; and the potential of our stereopure approach and nucleic acid therapeutics generally. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including the following: the ability of our preclinical programs to produce data sufficient to support the filing of INDs and the timing thereof; our ability to continue to build and maintain the company infrastructure and personnel needed to achieve our goals; the clinical results of our programs, which may not support further development of product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical studies; our effectiveness in managing future clinical trials and regulatory processes; the success of our platform in identifying viable candidates; the continued development and acceptance of nucleic acid therapeutics as a class of drugs; our ability to demonstrate the therapeutic benefits of our stereopure candidates in clinical trials, including our ability to develop candidates across multiple therapeutic modalities; our ability to obtain, maintain and protect intellectual property; our ability to enforce our patents against infringers and defend our patent portfolio against challenges from third parties; our ability to raise additional capital as needed; and competition from others developing therapies for similar uses, as well as the information under the caption "Risk Factors" contained in our Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on March 30, 2016 and in other filings we make with the SEC. We undertake no obligation to update the information contained in this press release to reflect subsequently occurring events or circumstances.

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